Remarks/Arguments

Claims 1-30 were of record. New claims 31-34, directed to a 0.1% strength diclofenac sodium composition, are presented. Claim 31 is directed to a composition of the invention "consisting essentially of" 0.1% diclofenac sodium and the recited excipients. Claims 32, 33 and 34 are each directed to the compositions "consisting of" 0.1% diclofenac sodium and the formulation excipients utilized in Examples 1, 2 and 3 of the specification, respectively. Accordingly, claims 1-34 are under consideration.

Objection,

The abstract of the disclosure was objected to "because of the use of legal phraseology 'said' in the second line." Accordingly, the abstract has now been amended by cancellation of 'said' and replacement with 'the', as well as by cancellation of the word "the" preceding "diclofenac sodium salt". A replacement page 10 containing the amended abstract is appended hereto.

Additionally, the Examiner's indication of a preference for section headings (Office action at pages 3-4) has been noted; and appropriate insertions will be made in the specification in due course.

35 USC 112, second paragraph.

The typographical error noted by the Examiner in claim 16 has been corrected by amendment of claim 16 to depend from claim 15 rather than cancelled claim 1, and accordingly the 112 rejection of record has been mooted.

35 USC 103

Rejection over Asche et al.

Claims 15-23 and 25-30 of record were rejected under this section over Asche et al., U.S. Patent No. 4,917,886 ("Asche et al."). Applicant respectfully traverses this ground of rejection.

Applicant's claims are all directed to "low-dose" topical emulsion gel compositions comprising the active pharmaceutical ingredient --namely, the sodium salt form of diclofenac--in a concentration of no greater than 0.4% (claims 15, 19), and preferably no greater than 0.1% (new claims 31-34). The compositions of the invention are "low-dose" relative to prior art compositions comprising diclofenac or its salts at concentrations of generally 1% or higher.

The claimed "low-dose" formulations arise from studies undertaken by the assignee of the present application indicating that topical emulsion gel formulations comprising concentrations of

either 1, 0.5 or 0.25% of diclofenac sodium as active ingredient are not statistically significantly different in relieving the symptoms of UV-induced skin reaction; and furthermore that 0.1% is the minimal effective concentration for a topical diclofenac sodium emulsion gel formulation for such indication (see, e.g., Kienzler et al., *Skin Pharmacol Physiol* 2005; 18: 144-152; and Magnette et al., *Eur. J. Dermatol* 2004:14:238-46, (copies enclosed)). Thus the diclofenac formulations of the invention have the distinct advantage of providing similar relief and healing as higher dose formulations of the prior art (e.g., 1% or greater), but with reduced exposure of the body to the active substance.

Diclofenac sodium salt is an active that is prone to crystallization (see applicant's published application, US2005/0239894, at Par. 4; and Sekine et al. at col. 1, ll. 57-61) as well as chemical degradation in the presence of typical emulsion gel excipients. Thus, in order for applicant to achieve practical application of a "low dose" diclofenac regimen for treating sunburn, applicant had to overcome the technical hurdle of stably formulating the diclofenac sodium to a very high standard in order to prevent it from falling to sub-therapeutic levels in the formulation (see '894 publication at col. 7). This technical hurdle involved selecting appropriate excipients in the necessary amounts so as to (1) maintain the drug in dissolved form, essentially free of crystal formation, so that it could permeate through the skin, while also (2) preventing esterification or other chemical degradation of the drug in the dissolved state. At the reduced levels of the active, this is a difficult "balancing act" that is nowhere taught or suggested by the cited art.

The cited Asche et al. reference was acknowleged in applicant's specification (see '894 publication at Par. 2). Asche et al. does generally disclose an emulsion gel preparation for diclofenac salts. However, the single formulation proposed by this reference for the sodium salt form of diclofenac requires the presence of diethanolamine as a neutralizing agent of the Carbopol gel-former ('894 publication, col. 2, l. 56 - col. 3, l. 6 934). Similarly, the working examples of Asche et al. utilize the diethylammonium or triethanolammonium salt forms of diclofenac, and all rely on an organic amine to neutralize the gel-forming agentv (see Asche et al. Examples 1-4). However, a significant problem with the Asche approach, as explained by applicant in the specification, is that diethanolamine is disfavored for use in topical pharmaceutical formulations by certain regulatory authorities due to safety concerns related to potential nitrosamine formation (see '894 publication at Par. 003).

Thus the present formulations differ from Asche et al. in providing an emulsion–gel form of diclofenac sodium without use of diethanolamine or other added organic amine neutralizing agents ('398 publication at Par. 3). Another difference between the subject matter of applicant's claims and Asche et al., is that the reference is concerned exclusively with higher dose concentrations, i.e. on

the order of 1% and higher, whereas applicant's formulations are directed to a "low dose" formulation that must meet a more rigorous standard of stability.

It was not obvious from Asche et al. that a stable "low dose" diclofenac sodium salt formulation prepared in the absence of added organic amines, was technically feasible. It is applicant's own discovery that by selecting the claimed excipients in the claimed ranges, it is possible to prepare stable "low dose" diclofenac sodium emulsion gel formulations in the absence of added organic amines, in which the drug is maintained at a therapeutic level, without loss due to crystallization or degradation. There is nothing in Asche that renders obvious applicant's particular selection of excipients, and certainly not the specific formulations of new claims 31-34 that "consist of" the excipients of applicant's working examples.

Accordingly, it is respectfully submitted that Asche et al. does not suggest either the desirability of a low-dose diclofenac sodium composition or how to prepare such a composition so that the drug is stably maintained at a therapeutic level, and accordingly the rejection of record of claims 15-23 and 25-30 should be withdrawn.

Rejection over Asche et al. and in view of Sekine et al.

Claim 24, directed to a composition which is expressly provided to be free of a C_{2-4}alkanol, was rejected under 35 USC 103 as being unpatentable over Asche et al. as applied to claims 15-23 and 25-30, and further in view of Sekine et al., U.S. Patent No. 6,054,484 ("Sekine et al."). Applicant's cancellation of claim 24 obviates this ground of rejection.

Summary.

Accordingly, reconsideration and withdrawal of the rejection of claim 16 under 35 USC 112, second paragraph, and the rejection of claims 5-23 and 25-30 under 35 USC 103, and allowance of claims 5-23 and 35-34, are respectfully solicited.

Should the Examiner believe that a telephonic interview with applicant's undersigned attorney would advance the status of this prosecution, she is respectfully invited to contact the undersigned at the below-indicated telephone number.

Other Fees.

Applicants request that any additional claim fees, or other fees necessitated by this paper, be charged to Deposit Account No. 50-4395 in the name of Novartis Consumer Health, Inc.

Respectfully submitted,

Diane Furman

Novartis Consumer Health Inc.
200 Kimball Drive
Parsippany, NJ 07054-0622
(973) 503-7050

Diane Furman
Attorney for Applicant
Reg. No. 31,104

Date: 29 April 2008

Enc: substitute "Abstract" page 10 of specification